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Case Report

The Diagnosis of Osteolymphoma: A Case Report and Review of the Literature
原發性非何傑金氏骨惡性淋巴腺癌的診斷: 病例報告及文獻回顧

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ABSTRACT

Osteolymphoma, also known as primary non-Hodgkin's lymphoma of the bone, is an unusual disease which can be difficult to diagnose. This case study concerns a 51-year-old patient who presented with right leg pain initially diagnosed as osteomyelitis. Failure of treatment and further investigation revealed an unusual primary tumour. We review the sequence of events leading to the diagnosis of osteolymphoma and the literature relating to the diagnosis.

中 文 摘 要

骨惡性淋巴腫瘤，也是被稱為原發性非何傑金氏骨惡性淋巴腺癌，是很難被診斷出的一種異常的疾病。 這案例是一位51歲病患者起初期有右腿痛礎，經過初步治療失敗後而作進一步的檢查而診斷出為原發性骨惡性淋巴腫瘤。我們討論診斷出骨惡性淋巴腫瘤的時序及評論有關係的文獻。

Introduction

Osteolymphoma[1] (OL) is an uncommon disease that can have an indolent course and so has the potential to be misdiagnosed, as in the case presented below. Also known as Primary Non-Hodgkins Lymphoma of Bone, OL is a discrete clinical entity that behaves differently to other lymphomas. We present a case that was difficult to both diagnose and manage, and review the literature relating to this emerging entity.

Case Report

The patient, a 51-year-old man, initially presented to his local medical officer with right leg pain 4 years ago. Plain radiographs of the right knee were reported as normal, and the left knee was said to have a mild effusion. No specific treatment was started.

The pain worsened over 6 months and culminated in a visit to the emergency department at the Tweed Hospital. The patient complained of a minor contusion to the leg which he knocked against a ladder. He also had redness of the overlying skin. His pain was worse at night, aggravated by standing, and improved by rest.

On examination, he had erythema and percussion tenderness over the shaft of the right tibia. He was able to weight bear on the limb, but with pain. The levels of his white blood cells, erythrocyte sedimentation rate (ESR), and C-reactive protein were normal and remained normal throughout the subsequent course of the disease. The orthopaedic registrar diagnosed osteomyelitis. The patient was admitted to hospital, and intravenous antibiotics were administered for 48 hours. He was discharged with oral antibiotics which he ceased taking after 2 weeks, because of no effect on his pain.

Two months later, the patient presented to his local medical officer again with persistent pain. The patient was then referred to the orthopaedic surgeon (G Freeman). Plain radiographs (Figure 1) of the right tibia suggested a proximal and mid-shaft cortical lesion. Computed tomography suggested periosteal reaction and trabeculation but no cortical erosion. Given the normal inflammatory markers, the diagnosis of osteomyelitis was discarded. The surgeon's differential diagnoses included neoplasm, and therefore further tests were arranged.

A bone scan showed diffuse uptake of isotope at the right tibia and a lesser but some abnormal uptake at the left tibia. Magnetic Resonance imaging demonstrated the presence of a cortical sinus and periostitis which was suggestive of chronic low-grade osteomyelitis of the right tibia. The left tibia was also shown to be involved.

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Figure 1. Plain radiograph of right tibia showing proximal lucency (7 November 2002).

A second opinion was sought from another radiologist who suggested adamantinoma. The patient was referred to a tertiary orthopaedic oncology unit for open biopsy. A specimen was retrieved from an area close to the midshaft of the right tibia (December 2002). Microscopy showed necrotic marrow and white cells in the centre of the sample, with bacterial cocci more superficially. Culture failed to isolate an organism. There were no neoplastic cells seen. The finding of cocci seemed to support the diagnosis of infection and, in the context of absence of neoplastic cells, antibiotics were recommenced.

The antibiotics did not change the patient's condition, and he was still suffering the same pain 1 year later. Further imaging was arranged. These reports stated that the periostitis had improved, and therefore the lesion was less likely to be infectious. A new diagnosis of osteofibrous dysplasia was suggested.

The blood tests were repeated, and electrophoresis demonstrated the presence of a paraprotein. The patient was then referred to a local haematologist who arranged a trephine of the iliac crest. This failed to show the presence of a neoplasm. A repeated magnetic resonance study showed that the lesion on the right had advanced proximally (Figure 2). Another radiologist was consulted; he suggested that infection was unlikely and the first open biopsy might have been harvested from a site where the disease was not active.

Finally, the orthopaedic surgeon (G Freeman) took a second open biopsy from the margin of the lesion. Macroscopically, the sample was composed of both bright red marrow and normal yellow marrow, with a clear demarcation between the two areas. This specimen demonstrated preservation of bony architecture and sheets of small mature lymphoid cells. Immunotyping revealed a low-grade unclassified B-cell lymphoma (Figure 3).

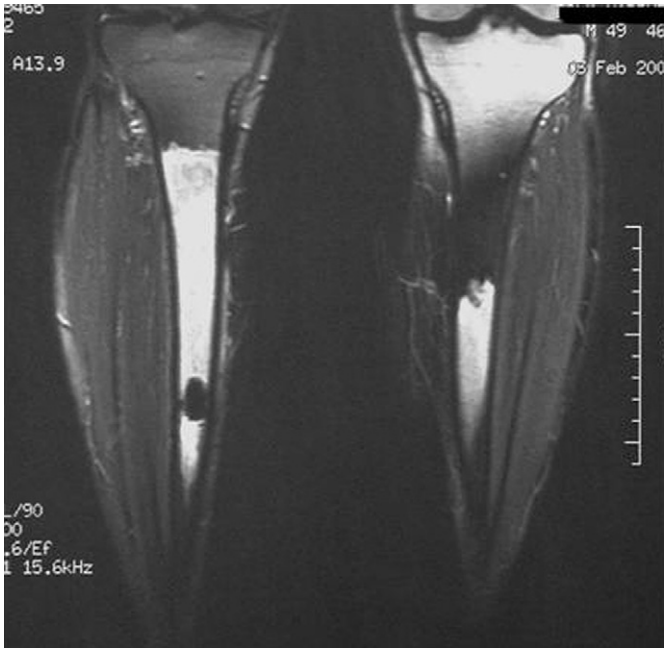

Figure 2. Coronal fat-saturated magnetic resonance image of the tibiae showing clear demarcation of the tumour. The initial biopsy site can be appreciated just below the midshaft of the right tibia.

The patient was referred to a radiation oncologist who revised the diagnosis to osteolymphoma (OL). The patient had 30 grays in 10 fractions over the course of 2 weeks. The patient continues to have pain and feels generally unwell after the treatment.

Discussion

Osteolymphoma (OL) is the name proposed by the Trans-Tasman Radiation Oncology Group[2] to standardise terminology. The disease has been known as primary non-Hodgkin's lymphoma of the bone, reticulum cell sarcoma, bone lymphoma, primary bone lymphoma, and primary skeletal lymphoma.[1]

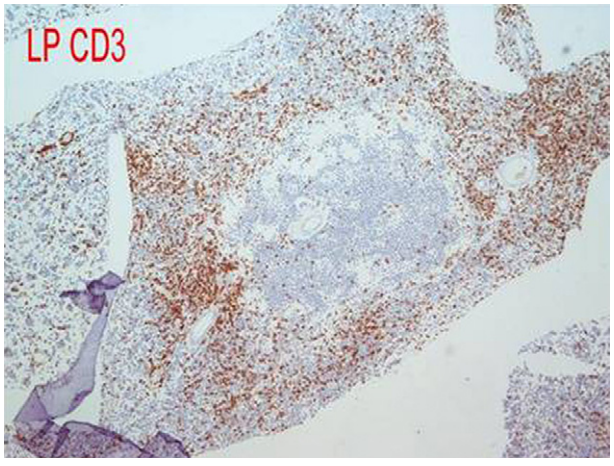

Figure 3. Low-power micrograph from second open biopsy. Cells have been stained with immunological marker for cell surface protein CD3, a T-cell surface antigen. Cells bound to the CD3 marker carry a red stain. The rapidly dividing, densely packed mass of lymphocytes at the centre of the field has not stained for CD3, which suggests that they are B cells. The picture may represent a T-cell immune response to a B-cell tumour, or mixed tumour of T and B cells.

OL is an uncommon disease, comprising 2–5% of primary bone tumours and less than 1% of all lymphomas.[3] A series shows female preponderance,[4] another study showed nearly even numbers,[5] but the largest series shows male preponderance.[6] There may be a bimodal distribution of the age of presentation.

The definition of OL includes only Ann Arbor Stage I and II disease. These patients have disease limited to bone and local ipsilateral lymph nodes at the time of diagnosis.

OL behaves differently from other lymphomas. It often presents in multiple sites, though this confers a relatively favourable outlook compared with disseminated disease originating elsewhere. Furthermore, OL presents and recurs exclusively in bones.[1]

Important differential diagnoses include osteofibrous dysplasia and adamantinoma.

The commonest symptom of OL is local bone pain and swelling.[6] The thoracic and lumbar spine are most affected, and then the femur, ribs and humerus.[5] Patients with spinal involvement usually had neurological symptoms. None of the patients had high-grade disease.

Blum et al[7] found a patient with a fluctuant cyst-like mass containing purulent material overlying the skeletal lesion. Another patient had an old open fracture at the lesion, whereas the third patient had a pathological fracture at the site of an aggressive high-grade large cell OL. The authors describe the confusion caused by the histological finding of numerous white cells, which led to the erroneous diagnosis of osteomyelitis.

Eighteen Canadian patients presenting over a period of 5 years[8] had localised bony pain and mostly normal initial blood tests, six having an increase in ESR. The authors also had difficulty in acquiring an accurate diagnosis with biopsy. They also highlighted the similar clinical pictures of OL and osteosarcoma, but the treatment for OL is non-surgical meanwhile osteosarcoma often requires excision.

An American series over 30 years identified 15 paediatric cases.[2] Their patients presented with painful, tender, palpable masses, and occasionally fever and malaise when the disease was disseminated. Three of these patients required more than one biopsy to establish the diagnosis. In another series, 9 of 14 patients required two biopsies to establish the diagnosis of OL.[9]

A German series[10] described two young patients presenting with bony pain and swelling at the tibia. Neither had systemic symptoms, and both had almost normal blood tests except that the female had a raised ESR. Both were found to have high-grade disease.

In conclusion, OL is an unusual disease with an indolent course, 50% of patients with unifocal disease being alive at 20 years.[6] Diagnosis can be a challenge. Trephine biopsy can be misleading. Repeated open biopsies should be considered.

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